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# Expression and significance of MMP-7, c-Jun and c-Fos in rats skin photoaging

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ABSTRACT

**Objective:** To investigate the expression and significance of the MMP-7, c-Jun and c-Fos in rat photoaging skin. **Methods:** A total of 45 SD rats were randomly divided into control group, model group, natural recovery group, physiological saline injection group and dermal pluripotent stem cells transplantation (DMSCs group), model group, natural recovery group, physiological saline injection group. DMSCs were treated with UV lamp irradiation to establish light aging skin model. Rats were then sacrificed after model prepared, no treatment was processed in the natural recovery group. Saline injections was adopted in saline group, DESCs group was treated with DESCs transplantation. Rats were sacrificed after 4 weeks. The expression of MMP-7, c-Jun and c-Fos were detected using the immunohistochemical method. **Results:** In model group, MMP 7 positive expression was higher than that in the other 4 groups, but without statistically difference ($P>0.05$); c-Jun, c-Fos expression were higher than that in the control group and DESCs group ($P<0.05$), there was no significant difference comparing natural recovery group with physiological saline injection group ($P>0.05$). **Conclusions:** MMP-7, c-Jun and c-Fos can be used as diagnosis indicators in the early stage of light aging, and they jointly participate in its development. DMSCs transplants is effective in treating light aging skin.

## 1. Introduction

Skin photoaging refers to the skin damaged by long exposure under ultraviolet light. The most common change is reduction of the collagen bundles in the dermis degeneration of elastic fibers. Serious light injury may cause skin cancer. Skin photoaging has become one hot research spot[1]. Current treatments commonly include drugs, physical, and surgical treatment, but they cannot fundamentally reverse the pathological physiology of the light ageing[2]. Studies have suggested that MMP-7, c-Jun and c-Fos may be involved in the occurrence and development of skin photoaging[3]. This study aims to explore the relationship of MMP-7, c-Jun, c-Fos with light skin aging.

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## 2. Materials and methods

### 2.1. Experimental animals

A total of 45 SD rats of 10 weeks, weighting (220±10) g, with SCXK qualified number 2007-005 were provided by the laboratory animal center.

### 2.2. Methods

#### 2.2.1. Model establishing

About 5-6 cm size area of rats back hair was cut off, the bare skin was exposed under 15 w UVA and UVB lamp irradiation for 2 h a day. After 100 d, the irradiated skin was

exacted under anesthetia, HE, VG staining were performed on the skin to establish photoaging model.

### 2.2.2. Experiment method

The rats were randomly divided into normal control group, model group, natural recovery group, physiological saline injection group and DESCs group, with 9 rats in each group. Rats were sacrificed after modeling, and the expressions of MMP-7, c-Jun, c-Fos in the lesion tissues were detected. Rats in natural recovery group did not undergo any intervention treatment, and they restored naturally. Physiological saline injection at same dosage was injected to the skin area daily in normal saline group. DESCs group rats were treated by DESCs transplantation to adjust the density of DMSCs to $1\times10^6$/mL, followed by deep dermal injection into skin photoaging area.

### 2.3. Indexes observation

After 4 weeks, rats were weighed and sacrificed, the lesions area skin were treated with formaldehyde fixation. They had paraffin embedding. They were cut into 6-9 slices serial section, and backed for 2 h in oven at 70 ℃. Expression of MMP-7, c-Jun and c-Fos of light aging lesions were detected by using SABC immunohistochemical method.

### 2.4. Statistics analysis

SPSS 17.0 software was used, and data was analyzed by using $t$ test. Data were expressed as mean±SD , $P<0.05$ was considered as statistically significant difference.

## 3. Results

### 3.1. MMP-7, c-Jun, c-Fos expression in different groups of rats

MMP-7 in skin tissue of model group presented brown or brownish red in colour; there was no significant difference in MMP-7 expression between model group and control group, natural recovery group or DESCs group ($P>0.05$). c-Jun, c- Fos were positively expressed in cutin cell nuclei except for the cuticle in light aging group. In the control group and DESCs group, c-Jun was restricted to granular layer, while in natural recovery group and physiological saline injection group, in addition to the particle layer, base layer and stratum spinosum also showed weakly positive expression of c-Jun. c-Jun, c-Fos expression in the model group was higher than the control group and DMSCs group; c-Jun, c-Fos expression showed more significant difference between model group and the control group ($P<0.05$). Compared with natural recovery group and physiological saline injection group, MMP-7 expression increased but the difference between groups was not statistical significant (P >0.05) (Table 1 and Figure 1-3).

**Table 1**

Average optical density value of immunohistochemical staining.

| Group | MMP-7 | c-Jun | c-Fos |
|---|---|---|---|
| Control group | 0.116±0.043 | 0.084±0.076 | 0.200±0.051 |
| Model group | 0.164±0.076 | 0.281±0.056 | 0.353±0.093 |
| Physiological saline injection group | 0.135±0.021 | 0.191±0.161 | 0.351±0.052 |
| DESCs group | 0.105±0.035 | 0.151±0.078 | 0.214±0.026 |

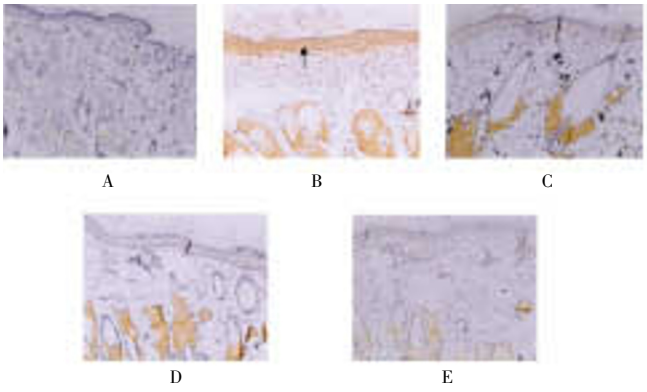


**Figure 1.** Expression of MMP-7 proteins in rats skin lesions tissue (× 200).
A: Control group; B: Model group; C: Natural recovery group; D: Physiological saline injection group; E: DESCs group.

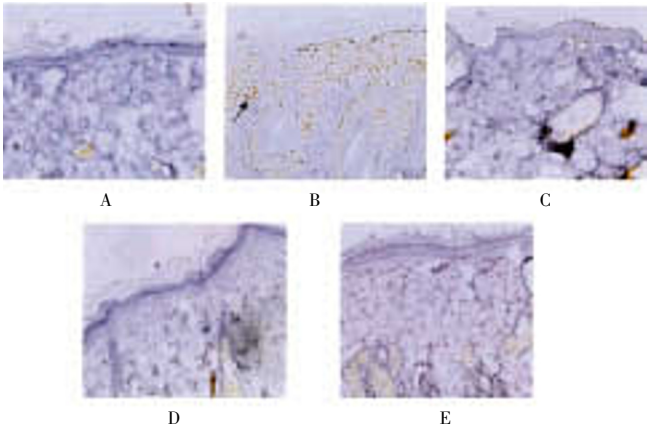


**Figure 2.** Expression of c-Jun proteins in rats skin lesions tissue (× 200).
A: Control group; B: Model group; C: Natural recovery group; D: Physiological saline injection group; E: DESCs group.

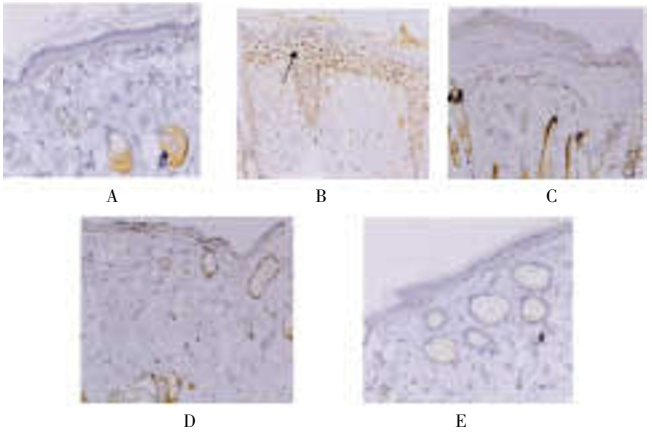


**Figure 3.** Expression of c-Fos proteins in rats skin lesions tissue (×200).
A: Control group; B: Model group; C: Natural recovery group; D: Physiological saline injection group; E: DESCs group.

### 3.2. Photoaging skin changes after DMSCs treatment

After DMSCs transplantation treatment, skin desquamation and pigment spots were relieved in DMSCs group significantly. Symptoms were improved; texture was narrowed and lightened, compared with model group. The elasticity restored to normal status.

## 4. Discussion

Skin photoaging is caused mainly by visible light waves in 400-800 nm, ultraviolet UVA of long wave, UVB of medium wave, ultraviolet rays UVC UVB and UVC of short wave. These light spectrums can cause skin damage, and longer wavelength can cause severer penetrating effect[4,5]. Studies have found that[6], severe irradiation of UVA, UVB can make skin erythema and vascular injury. UVB can change the structure of DNA, making the original oncogene activated and tumor-suppressor gene inactivated, and UVA can cause secondary damage of DNA generated by peroxide, participating in the occurrence of skin photoaging together.

MMP-7 is rarely expressed in normal tissues, expression quantity rises in malignant transformation process of the tumor stromal cells, inflammatory cells and epidermal cells. It is higher in benign tumor than that in normal tissue, but lower than that in malignant tumor tissues, showing that it plays an important role in the process of malignant[7]. Studies have reported[8], after UVA/UVB irradiation for 3 d, MMP-7 can be detected in the sweat gland epithelial cells, but not in the normal skin tissue. In this study, MMP 7 shows positive expression lesions in basal cell layer, the stratum spinosum and in the cytoplasm of the sebaceous glands, sweat gland in model group, consistent with literature reports. And in model groups, MMP-7 expression level was higher than the control group and DESCs group, suggestinging that MMP 7 may cause cancer gene expression related with skin light aging.

c-jun, c-Fos are nuclear proto-oncogenes, and showed no expression or low expression in the normal skin tissue. As stimulation, they are expressed rapidly. The proteins transmit and integrate information through the expression of c-jun and c-Fos, to change transcription level of genes[8]. Studies have reported that the excessive expression of c-Jun can reduce the expression of type I collagen, which is the most effective maintain cells against high mechanical tension. Collagen damages itself, and may reduce the synthesis of new collagen[9]. In this study, the expression of c-Jun, c-Fos in the model group is significantly higher than normal group and DESCs group ($P<0.05$), which is consistent with other reposrts[10]. Ultraviolet rays can activate and accelerate c-jun, c-Fos expression. In photoaging skin, c-jun and c-Fos form different sources dimmers for degradation of the dermal collagen and other matrix components. After DMSCs transplantation treatment, c-Jun, c-Fos expression decreased significantly in DESCs group, suggesting that DMSCs can reduce cutin forming cells c-Jun, c-Fos. It shows that DMSCs is ideal seed cells to slow down skin photoaging. There was no statistically significant difference between model group and normal saline injection, natural recovery group, showing that natural recovery and physiological saline stimulate light repair aging skin tissue without obvious effect. In this experiment, the c-Jim, c-Fos in sebaceous glands also accidentally showed weakly positive expression in the cytoplasm, this may be related to secretion of a small amount of the protein by sebaceous glands. MMP-7 expression is negatively correlated with c-jun, c-Fos, c-jun. c-Fos were positively correlated with c-jun[11].

This study showed MMP-7 correlates with c-Jun, c-Fos in the lesions of light aging skin. MMP-7, c-Jun and c-Fos involve in its development, and can be used as diagnosis indicators in early light aging. DMSCs transplantation has good therapeutic efficacy in treating light aging skin.

## Conflict of interest statement

We declare that we have no conflict of interest.

## References

[1] Lei XG, Li DT, Wang ZH. Dermal pluripotent stem cells transplantation treat big skin II light aging research. *Chin J Cosmetic Plastic Surg* 2010; **21**(8): 493-494.

[2] Tiemey EP, Hanke CW. Recent advances in combination treatments for photoaging: Review of the literature. *Deraiatol Surg* 2010; **36**(6): 829-840.

[3] Hunt DP, Jaholda C, Chandran S. Multipotent skin-derived precursors: from biology to clinical translation. *Curr Opin Biotechnol* 2009; **20**(5): 522-530.

[4] Zhong JQ, Hu NF, Li L. The research progress of relationship between dermal stem cells and skin aging. *Chin Skin Venereol Mag* 2010; **26**(5): 479-481.

[5] Zitka O, Kukacka J, Krizkova S, Huska D, Adam V. Matrix metalloproteinases. *Curr Med Chem* 2010; **17**(31): 3751-3768.

[6] Yu Y, Yang HF, Shao JJ. DAPI marks rat glioma model migration and positioning within bone marrow mesenchymal stem cells in the Glioma model. *J Tissue Eng Res Clin Reh Chin* 2010; **14**(23): 4243-4246.

[7] Li KJ, Hua G, Li H. Mechanism research progress and protection of light skin damage. *J Dermatol Venereol* 2010; **32**(4): 24-27.

[8] Quan TH, Qin ZP, Xu YR. Ultraviolet Irradiation Induces CYR61/CCNl, a mediator of collagen homeostasis, through activation of transcription factor AP-1 in human skin fibroblasts. *Inv Dermatol* 2010; **130**(6): 1697-1706.

[9] Guo BR, Liu P, Ma CC. The expression of c-jun, c-fos in light aging disease and significance. *Chin Skin Venereol Mag* 2009; **23**(12): 791-793.

[10] Zhang GH, Bo ZH, Chen T. The correlation research of skin photoaging molecular biology index and treatment. *J Inner Mongolia Med Coll* 2009; **31**(1): 10-14.

[11] Dunn KM, Lee PK, Wilson CM, Iida J, Wasiluk KR, Hugger M, et al. Inhibition of hyaluronan synthases decreases matrix metalloproteinase-7 (MMP-7) expression and activity. *Surgery* 2009; **145**(3): 322-329.